IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: AVANDIA MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	)	MDL NO. 1871
STACI LAURINO, *on behalf of herself and all others similarly situated,*	)	07-MD-01871
Plaintiff,	)	Case No. 12-cv-03683
v.	)	JURY TRIAL DEMANDED
SMITHKLINE BEECHAM CORPORATION D/B/A GLAXOSMITHKLINE (GSK)	)	
Defendant.	)	

AMENDED COMPLAINT

Plaintiff Staci Laurino, on behalf of herself and all others similarly situated, makes the following allegations pursuant to the investigation of her counsel and based upon information and belief, except as to allegations specifically pertaining to herself, which are based on personal knowledge.

NATURE OF THE ACTION

1. Pursuant to the Missouri Merchandising Practices Act, Mo. Rev. Stat. §§ 407.010 *et seq.*, ("MMPA"), Plaintiff brings this action against Defendant on her own behalf and as representative of the class for damages arising from their purchases of Avandia.

THE PARTIES

2. Plaintiff Staci Laurino is a citizen of the state of Missouri, residing in Saint Louis, Missouri. Plaintiff purchased and consumed Avandia within the jurisdiction of the United States District Court for the Eastern District of Missouri.

3. Defendant SmithKline Beecham Corporation is a foreign corporation doing business as GlaxoSmithKline ("GSK"). Defendant maintains its principal place of business at One Franklin Plaza; 200 North Sixteenth Street; Philadelphia, Pennsylvania 19102. At all times relevant herein, GSK was a pharmaceutical company doing business in the state of Missouri. Defendant also conducted business from its principal place of business in Pennsylvania.

JURISDICTION AND VENUE

4. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. § 1332(d) because there are more than 100 class members and the aggregate amount in controversy exceeds $5,000,000.00, exclusive of interest, fees, and costs, and at least one Class member is a citizen of a state different from Defendant.

5. Pursuant to 28 U.S.C. § 1391, venue is proper in the United State District Court for the Eastern District of Missouri because a substantial part of the events, omissions and acts giving rise to the claims herein occurred in that District. Plaintiff is a citizen of Missouri and Defendant, a foreign corporation with its principal place of business in Pennsylvania, has distributed, advertised and sold Avandia, which is the subject of the present Complaint, in that District.

6. In its Conditional Transfer Order dated June 19, 2012, the Judicial Panel on Multidistrict Litigation transferred this case to this Court for pre-trial proceedings under 28 U.S.C. § 1407. *See* Conditional Transfer Order [Doc. # 903].

FACTUAL BACKGROUND

Diabetes and Enhanced Cardiovascular Risks

7. Type II diabetes is a serious, life threatening disease and the most common form of diabetes, affecting approximately 18-20 million Americans. It occurs when the body becomes resistant to insulin. Insulin, made in the pancreas, is necessary to enable the transport of sugars

from bloodstream to cells. Without insulin, sugar builds up in the bloodstream and the cells are starved for energy. This can lead to kidney failure, blindness, amputations, heart attacks and stroke. When a patient's insulin resistance results in a fasting blood glucose in excess of 126 mg/dl for two consecutive days, the subject patient is classified as having Type II diabetes

8. Most people with diabetes have health problems or risk factors that increase the risk for heart disease and stroke. Cardiovascular disease is the leading cause of death for persons with Type II diabetes and more than 65% of persons with diabetes will die from a heart attack or stroke. *See* http://www.diabetes.org/type-2-diabetes/well-being/heart-disease-and-stroke.jsp. With diabetes, heart attacks occur earlier in life and often result in death. Thus, it is important to any diabetes treatment to reduce this cardiovascular risk. *See* Scott M. Grundy, et al. "Diabetes and Cardiovascular Disease, A Statement for Healthcare Professionals From the American Heart Association." *Circulation* 100:1134-1146 (1999).

9. During the past decade, numerous drugs have been introduced for the treatment of Type II diabetes that are supposed to better control the disease and reduce the health complications often associated with diabetes, such as heart attacks, strokes and other cardiovascular complications.

10. First manufactured in the 1990s, thiazolidinediones (TZDs) are a class of insulin-sensitizing antidiabetic agents, which work in part by increasing cell sensitivity to insulin. TZDs lower blood sugar levels and enable the body to more effectively use insulin by reducing insulin resistance in the body. In the United States, two TZDs are indicated for use in Type II diabetes mellitus: rosiglitazone and pioglitazone.

11. Defendant designed, tested, manufactures, promotes, distributes, labels, advertises, and markets Avandia Tablets, Avandamet Tablets, and Avandaryl Tablets within Missouri as well as nationwide.

12. Avandia was first approved for use in the United States in May 1999 for the use in treatment of Type II diabetes mellitus, also known as non-insulin-dependent diabetes mellitus ("NIDDM") or adult-onset diabetes.

13. Avandamet, a single pill combination of Avandia and metformin, was approved in October 2002 in the United States for use in treatment of Type II diabetes.

14. Avandaryl, a single pill combination of Avandia and Amaryl, was approved in November 2005 in the United States for use in treatment of Type II diabetes.

15. As used herein, the term "Avandia" refers to and includes Avandia, Avandamet, and Avandaryl.

Avandia Was Highly Profitable for GSK

16. At all relevant times, GSK was in the business of designing, testing, licensing, labeling, promoting, manufacturing, marketing, advertising, selling and distributing pharmaceuticals and other products, including Avandia, within Missouri and elsewhere.

17. GSK is licensed to do business and in fact does business by agent in the state of Missouri. At all relevant times, GSK designed, developed, licensed, marketed, manufactured, and sold Avandia, including the Avandia at issue in this lawsuit.

18. GSK did this throughout the United States, in the state of Missouri, and within the jurisdiction of the United States District Court for the Eastern District of Missouri.

19. The Avandia drugs were blockbusters for GSK. More than 6,000,000 people worldwide have taken these drugs since 1999, and Avandia has been used by at least one million individuals in the United States.

20. GSK's unlawful practices in connection with its marketing and sales of Avandia were highly successful, with U.S. sales of more than $1 billion in 2005 and more than $2 billion in 2006.

21. In 2007, Avandia sales were approximately $1.55 billion. As recently as 2009, Avandia sales topped $658 million, making Avandia a hugely successful drug for GSK.

22. GSK widely promoted the use of Avandia as a safe and effective method of treating type II diabetes mellitus since its launch. Yet GSK has known, or upon reasonable inquiry would have known, since at least as early as 1999 that Avandia caused an increased risk of heart attacks and death. Other studies also have concluded that Avandia is no more effective than other drugs.

Food, Drug, and Cosmetic Act and FDA Regulations

23. "Congress enacted the FDCA to bolster consumer protection against harmful products." *Wyeth v. Levine*, 555 U.S. 555, 574 (2009).

24. Under the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. §301 *et seq.,* drug manufacturers must obtain approval from the United States Food and Drug Administration ("FDA") before they can market any drug in interstate commerce. In the case of new brand-name drugs, approval from the FDA begins with a new-drug application (NDA) containing materials that must include "full reports of [all clinical] investigations" (§355(b)(1)(A)) relevant nonclinical studies, and "any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source." 21 C.F.R. §§314.50(d)(2) and (5)(iv) (2012). The NDA must also include "the labeling proposed to be used for such drug," 21 U.S.C. §355(b)(1)(F); 21 C.F.R. §314.50(c)(2)(i), and "a discussion of why the [drug's] benefits exceed the risks under the conditions stated in the labeling," 21 C.F.R. §314.50(d)(5)(viii); §314.50(c)(2)(ix). It is a

prohibited practice to introduce or deliver for introduction into interstate commerce any drug that is adulterated or misbranded. 21 U.S.C. §331(a). A drug is misbranded if it is dangerous to health when used in the dosage, manner, frequency or duration prescribed, recommended or suggested in the labeling (21 U.S.C. 352(j)), or if the label is false or misleading in any particular. 21 U.S.C. §352(a). The label must contain adequate warnings of dangers to health. 21 U.S.C. 352(f). Moreover, any advertisements must:

(a) Contain true statements of information relating to side effects, contraindications (including warnings and precautions) and effectiveness, including any qualification or pertinent information the absence of which would make any part or theme of an advertisement misleading. 21 U.S.C. § 352(n); 21 C.F.R. § 202.1(e)(1); 21 C.F.R. § 202.1(e)(3)(i); 21 C.F.R. § 202.1(e)(4)(ii).

(b) Contain fair balance between information related to contraindications and information relating to efficacy. *See* 21 C.F.R. § 202.1(e)(6); 21 C.F.R. § 202.1(e)(5). Advertisements containing favorable information or conclusions from a study inadequate in design, scope or conduct to furnish significant support for such information or conclusions, or that suggest that a drug is safer than has been demonstrated by substantial evidence or substantial clinical experience, or by selective presentation of information, are false, lacking in fair balance or misleading. *See* 21 C.F.R. § 202.1(e)(6); 21 C.F.R. § 202.1 (e)(7).

25. At all times before and after approval of Avandia, GSK had an obligation to provide a warning adequately describing Avandia's risks. GSK was required to fully and accurately disclose information relating to both Avandia's efficacy and adverse events associated with Avandia's use. *See* 21 U.S.C. §§ 331(a), 352(a), 352(n). The manufacturer "is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long

as the drug is on the market." *Wyeth*, 555 U.S. at 571 (citing 21 CFR § 201.80(e) (requiring a manufacturer to revise its label "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug"); § 314.80(b) (placing responsibility for postmarketing surveillance on the manufacturer); 73 Fed. Reg. 49605 ("Manufacturers continue to have a responsibility under Federal law . . . to maintain their labeling and update the labeling with new safety information"). GSK failed to accurately or fully describe Avandia's efficacy or risks in violation of sections 352(a), 321(n) and accompanying regulations.

Early Warnings That Avandia Was Unsafe and GSK's Efforts to Discredit Dr. Buse

26. Prior to approval, Avandia underwent a FDA Medical Officer Review, completed in April 1999. The reviewing officer stated: "The major issues regarding safety of rosiglitazone relate to hepatitis, edema, anemia and the heart." Robert Misbin, MD, "Medical Officer's Review of New Drug Application" at 26 (April 16, 1999).

27. The Review further stated: "Safety: The only safety issue noted in this study is that 6 patients on 4 mg bid had cardiac events including two myocardial infarctions." *Id.* The Safety/Cardiac Abnormalities Section of the Review also states: Acute myocardial infarctions occurred in 22 patients (0.5%) of patients on [Avandia] and was fatal in six. This result would appear somewhat higher than in other treatment arms." *Id.* at 28.

28. The reviewing officer stated that, as a condition of approval, GSK needed to conduct a post-marketing study to better assess this risk. *Id*. at 41.

29. GSK, however, resisted and did not undertake the study stating that it would be too much effort and too expensive. *See* Letter to Jena Weber from Clare Kahn re: NDA 21-071-Request for Revised Annotated Labeling and Outline of Phase IV Commitments dated May 5, 1999 ("given the scope, complexity, and expense of such trials [GSK] is not currently in a position to make any commitment about a long term outcomes trial.").

30. Soon after Avandia's 1999 approval, Dr. John B. Buse, former president of the American Diabetes Association, and head of endocrinology at The University of North Carolina at Chapel Hill School of Medicine, raised concerns about Avandia and heart problems, including the risk of heart attack and death. At the time that Dr. Buse discovered and reported his findings to GSK, he was an investigator for a GSK study on Avandia.

31. In a series of speeches in early 1999, including presentations to the Endocrine Society and the American Diabetes Association, Dr. Buse outlined his concerns about Avandia and the increased cardiovascular risks associated with the drug. *See* Committee Staff Report to the Chairman and Ranking Member, Committee on Finance, United States Senate, November 2007, "The Intimidation of Dr. John Buse and the Diabetes Drug Avandia."

32. Rather than attending to these warnings, GSK set out on a campaign to stifle Dr. Buse's findings, including threatening Dr. Buse with a lawsuit if he continued voicing his concerns about Avandia. *See* Dr. Buse's testimony before the Committee on Oversight and Government Reform, June 6, 2007.

33. Senior executives at GSK – including its Chief Executive Officer – were aware of the campaign to silence Dr. Buse. *See* Committee Staff Report to the Chairman and Ranking Member, Committee on Finance, United States Senate, "The Intimidation of Dr. John Buse and the Diabetes Drug Avandia," dated November 2007.[1]

34. In response to GSK's pressure, Dr. Buse sent a three-page letter to Dr. Tadataka Yamada, GSK's Chairman of Research and Development on or about June 29, 1999. In the letter, Dr. Buse wrote: "I may disagree with [GSK]'s interpretation of that data … I am not for sale … Please call off the dogs. I cannot remain civilized much longer under this kind of heat."

[1] Nearly eight years after Dr. Buse first raised red flags about Avandia, the Senate Committee determined in 2007 that GSK conducted an "orchestrated plan to stifle the opinion" of Dr. Buse.

35. On March 15, 2000, Dr. Buse wrote to Dr. Jane Henney, Commissioner of the FDA, stating that he was concerned that GSK had "overstated the safety of [Avandia] with respect to cardiovascular issues" because studies reflected a "worrisome trend in cardiovascular deaths and severe adverse events." *See* Buse Letter to Henney, FDA re: Citizen's Petition to Immediately Require Class Labeling for the Diabetes Drugs Troglitazone (Rezulin), Rosiglatzone (Avandia) and Pioglitazone (Actos), dated March 15, 2000.

36. Dr. Buse was not the only person to alert GSK to the increased risk of heart attack and death associated with Avandia. Shortly after Dr. Buse raised his concerns, Public Citizen filed a petition in March 2000 seeking immediate class labeling changes for all marketed TZDs, including rosiglitazone.

37. In an independent investigation of TZDs, Public Citizen, after studying reviews by FDA Medical Officers, Statisticians, and Pharmacologists, transcripts of FDA advisory committee meetings, and scientific literature on trolitazone, rosiglitazone, and rioglitazone, argued that information associating rosiglitazone to heart attacks and serious cardiovascular injuries "was never included in the label, or seriously understated." Sidney M. Wolf, M.D., *et al.*, *Petition Requesting Updated Labeling for Troglitazone (Rezulin), Rosiglitazone (Avandia) and Pioglitazone (Actos)*, Public Citizen (March 7, 2000) (available at www.citizen.org/Page.aspx?pid=1736).

38. Public Citizen cited studies submitted to the FDA that evidenced lack of efficacy. *See id.* at §§I(A) and I(B). Additionally, the studies demonstrated an increase in cardiovascular risks in animal studies, including the increased risk of suffering a heart attack. *Id.* at § II(B) ("In animal studies, the major toxic effect of all the drugs in the glitazone class was on the heart.") (also noting that five patients on rosiglitazone had "acute myocardial infarctions."). Based on

the studies, the Public Citizen report concluded that "[t]he potential deleterious effects on heart function are downplayed in the current label." *Id.* at § II(B).

39. Public Citizen's Petition concluded that product labeling for Avandia was "inadequate, misleading, and potentially dangerous" because safety concerns associated with the drug included "liver toxicity, effects on heart function, weight gain, edema, anemia, low blood pressure, elevated lipid levels, and possible changes in progesterone levels." *Id.* The Petition stated that the risks and efficacy concerns associated with Avandia "was never included in the label, or seriously understated" and that the "labeling omits important safety and efficacy information to such an extent that physicians are likely to prescribe these drugs inappropriately." *Id.*

40. There were other warnings as well. As reported in a November 19, 2008 *Wall Street Journal* article, Dr. Mary Money of Hagerstown, Maryland, observed problems with Avandia shortly after it entered the market in 1999 and attempted to warn GSK in 2000. According to this article, Dr. Money linked Avandia to congestive heart failure when an echocardiogram showed high pressure in the arteries of the lungs of a patient who had begun taking Avandia two weeks earlier.

41. Despite these early warnings from a variety of sources, GSK ignored them and took no steps to advise consumers of Avandia's risks. Indeed, independent of these other sources, GSK already was aware of early warning signs concerning Avandia. GSK conducted a study in 1999 "to find out if [Avandia] was safer for the heart than a competing pill . . ." Gardiner Harris, *Diabetes Drug Maker Hid Test Data, Files Indicate*, The New York Times July 13, 2010. According to the report, "instead of publishing the results, the company spent the next 11 years trying to cover them up." *Id.* In an internal email, a senior GSK executive said that

"Per Sr. Mgmt request, these data should not see the light of day to anyone outside of GSK." *Id.* Based on these documents, GSK "had data hinting at extensive heart problems almost as soon as [Avandia] was introduced in 1999." Again, GSK did nothing.

Additional Warnings About Avandia's Safety

42. In February 2001, the FDA required GSK to change its label to reflect a risk of heart failure observed in patients taking Avandia and insulin.

43. In a letter dated February 22, 2001, the FDA's Division of Drug Marketing, Advertising and Communications (DDMAC) informed GSK that all promotional materials for Avandia should be revised to prominently include the risks, no later than March 8, 2001.

44. Instead of complying with FDA requirements, GSK's sales representatives engaged in false or misleading promotional activities with respect to the risk information in Avandia's product labeling.

45. In a Warning Letter dated July 17, 2001, the FDA stated that GSK had engaged in continued violation of federal regulations in its promotional activities for the marketing of Avandia.

46. In that Warning Letter, the FDA also warned that GSK was continuing to market Avandia improperly because its representatives at a conference "made oral representations denying the existence of serious new risks associated with Avandia at [GSK]'s promotional exhibit booth." Furthermore, the FDA concluded that GSK's promotional exhibits were non-compliant.

47. The FDA's letter concluded:

> Your promotional activities that minimize serious new risks are particularly troublesome because we have previously objected, in two untitled letters, to your dissemination of promotional material for Avandia that failed to present any risk information about

> Avandia or minimized the hepatic risk associated with Avandia. ***Despite your assurances that such violative promotion of Avandia had ceased, your violative promotion of Avandia has continued.***

48. In February 2002, GSK submitted a supplemental New Drug Application (sNDA) seeking approval for use of Avandia in combination with insulin. In response, the FDA asked GSK to submit additional information regarding adverse events from follow-up trials. Upon review of this information, the FDA noted that results showed that "approximately 10% of patients treated with rosiglitazone and insulin experienced cardiac [adverse events] across the trials to date." Memorandum from FDA re: NDA review issues and recommended action, dated February 26, 2003.

49. The FDA also noted that, given earlier signals, an increase in cardiovascular risk was not unexpected, stating: "[W]hile the signal of increased risk for edema, [congestive heart failure], and other [cardiovascular] adverse events persists in these follow up trials (indeed, there was no expectation that it was a fluke of the earlier trials and would disappear in subsequent studies), a strategy of careful patient selection (e.g., no history of cardiac compromise), judicious titration, and monitoring may obviate some of the fluid-related [adverse events] of the combination." *Id.*

50. The FDA's Medical Team Leader stated that "there was a marked increase in total adverse cardiac events, serious adverse cardiac events, and adverse cardiac events leading to withdrawal in patients on insulin and Avandia combination therapy when compared to insulin alone . . . ." Memorandum from the Medical Team Leader to the Division Director at the FDA re: Team Leader Recommendation.

51. The FDA's Medical Team Leader recommended against approving GSK's application for combination therapy with insulin, stating that "although the sponsor has shown

that Avandia is effective in providing better glucose control when added to insulin, the safety information that emerged from the studies is quite troublesome." *Id.* The Medical Team Leader also recommended that GSK consider sending a letter to doctors warning of the dangers associated with combining Avandia and insulin therapies.

52. In April 2006, the FDA required labeling for Avandia to be updated to include new data in the Warnings Section about a potential increase in heart attack and heart-related chest pain. This change was based on the results of a controlled clinical trial in patients with existing congestive heart failure. A higher number of heart attacks or angina was observed in patients treated with Avandia compared to those treated with placebo.

GSK- and Industry-Sponsored Studies Revealed Risks Concerning Avandia

GSK's Early Trial Studies

53. In 2005, GSK commissioned an observational trial study that was conducted in two parts: the first in 2005 and the second in 2006. This study was designed to be a meta-analysis, meaning that it combines the result of several studies that address a set of related research hypotheses.

54. The analysis of the first trials was completed during the fall of 2005. These trials resulted in a hazard ratio for myocardial ischemia of 1.29, meaning that Avandia increased the risk of heart-related ischemia by 29 percent.

55. The analysis of the second trials was completed in the summer of 2006. Similar to the first trials, the second trials found an enhanced hazard ratio of 1.31.

56. Both of these results are statistically significant and provided further notice, or at minimum, demonstrated the serious need for further true investigation of the cardiovascular risks associated with Avandia.

57. Despite these indicators for adverse cardiovascular effects, GSK did not disseminate the results of its tests. GSK's Chief Executive Officer said, "Why would you publicize it? . . . We don't publicize every submission we make to the [FDA]." Andrea Gerlin, *Glaxo, Top Ad Spender, Didn't Publicize Avandia Risks (Update 4)*, Bloomberg News June 1, 2007.

RECORD

58. In an attempt to support Avandia and discredit other study results, GSK sponsored a 4,447-patient study called RECORD. On June 5, 2009, GSK released purported results from RECORD showing no difference in the rates at which patients were hospitalized for or killed by heart disease whether they were on a drug combination that included Avandia or not. But the paper detailing the results "was missing a key fact: 40% of patients analyzed in the study were not taking Avandia at the study's end." Matthew Herper, *Glaxo Fails To Learn The Lesson Of Avandia*, Forbes June 5, 2009. The fact that so many RECORD participants were no longer taking Avandia was "key information because it means side effects could be washed out by the number of patients who were included in the final tally but weren't on the drug." *Id.* Also, "patients on Avandia took 10% more cholesterol-lowering drugs, which reduce the rate of heart attack . . . [making] the trial worthless." *Id*. (quoting Dr. Nissen). Nonetheless, despite these fundamental flaws with RECORD and GSK's failure to disclose critical facts about RECORD, GSK touted the study in an effort to "exonerate[] its Avandia diabetes pill of the charge that it raises the risk of heart attack." *Id.*

59. Given these shortcomings, Dr. Thomas Marciniak from the FDA denounced RECORD and its conclusions. Dr. Marciniak concluded that "RECORD was inadequatley designed and conducted to provide any reassurance about the cardiovascular safety of [Avandia],

RECORD confirms and extends the recognized concerns regarding heart failure and heart failure deaths with [Avandia], and RECORD suggests that [Avandia] increases the risk for myocardial infarction." Thomas A. Marciniak, M.D., Div. of Cardiovascular and Renal Products Food and Drug Administration, *Cardiovascular Events in the RECORD Trial*. Dr. Marciniak "found a dozen instances in which patients taking Avandia appeared to suffer serious heart problems that weren't counted in the study's tally of adverse events" and that such discrepancies "suggest serious flaws with trial conduct." Gardiner Harris, *FDA Review Slams Avandia Study That Omitted Heart Failures*, The Seattle Times July 9, 2010.

DREAM and ADOPT

60. Subsequently, after the FDA began instituting regulatory reforms for Avandia, GSK sought to justify keeping Avandia on the market with the results of two industry sponsored studies – DREAM and ADOPT – which GSK claimed did not show a significant cardiovascular risk.

61. The FDA Joint Advisory Committee, however, recognized that these studies did not in fact "study the patients of interest, and in fact, excluded the patients that we are concerned about," *i.e.*, persons with diabetes, and thus did not necessarily inform decisions regarding risk for Avandia. Summary Minutes of the Joint Meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee, July 30, 2007, at 5.

62. The DREAM study "recruited a low-risk population of prediabetic patients to evaluate whether rosiglitazone, as compared with placebo, could prevent the chemical onset of diabetes." Psaty and Furberg, "The Record on Rosiglitazone and the Risk of Myocardial Infarction," *NEJM*, 357:67-69 (July 2007).

63. Indeed, even among the pre-diabetes study population, the DREAM results indicated increased cardiovascular risks. Dr. Nissen called the results "very disturbing," stating that "despite a substantial delay in onset of diabetes, rosiglitazone resulted in a 37% increase in adverse cardiovascular events, a finding that very nearly reached conventional levels of significance. This trend virtually precludes the possibility of an overall benefit and suggests an unexpected mechanism for harm. Rosiglitazone is known to increase concentrations of LDL cholesterol." *The Lancet*, Vol. 368, Issue 9552 at 2049, December 9, 2006.

64. The ADOPT study also had "several weaknesses in design and conduct." Psaty and Furberg, "The Record on Rosiglitazone and the Risk of Myocardial Infarction," *NEJM*, 357:67-69 (July 2007). Among other things, GSK was faulted for failing to "make a serious effort to verify the presumed health benefits of rosiglitazone in a timely fashion. In ADOPT, which compared rosiglitazone with metformin and glyburide in terms of the duration of glycemic control, cardiovascular events were not identified or recorded in a systematic fashion, and heart failure was the only outcome that was reviewed and adjudicated at the end of the trial. Nonetheless, even though misclassification and incomplete ascertainment of events effectively reduce the ability of a study to detect a difference in event rates, rosiglitazone in ADOPT was associated with *a higher risk* of cardiovascular events, including heart failure, than glyburide [the comparator drug]." *Id.* (emphasis added)

65. As reported in the *NEJM*, results of prior studies "still suggest[ed] that rosiglitazone is associated with an increased risk of myocardial infarction" and "the possibility of a benefit in terms of the risk of myocardial infarction remains remote, and there is still significant evidence of harm." *Id.*

66. Moreover, "rosiglitazone was approved on the basis of its ability to improve glycemic control, a surrogate end point. Because high glucose levels increase the risk of vascular disease, a glucose-lowering drug is presumed to reduce the risk of major adverse health outcomes such as myocardial infarction. Rosiglitazone, however, appears to be associated with an increase rather than a decrease in the risk of myocardial infarction." *Id.*

67. The *NEJM* reported that "[t]he DREAM trial and ADOPT focused largely on marketing questions and failed to address questions of myocardial infarction–related risk or benefit directly. These industry-sponsored trials do not represent compelling science." *Id.*

The Nissen/Wolski Study

68. In May 2007, *The New England Journal of Medicine* (*NEJM*) published a meta-analysis conducted by Dr. Steven Nissen and Kathy Wolski entitled "Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes" (the "Nissen/Wolski Study").

69. The Nissen/Wolski Study reviewed data available to them through published literature, the FDA website, and Defendant's clinical-trials registry. The analysis included a review of 42 clinical trials involving nearly 28,000 patients.

70. The Nissen/Wolski Study concluded that "[r]osiglitazone was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from cardiovascular causes that had borderline significance." *Id.*

71. The study found that a diabetic taking Avandia has a much greater risk of suffering a heart attack or serious cardiovascular event – an estimated 43% increase or greater – when compared with other diabetes drugs or placebos. *Id.* People taking Avandia suffered such adverse events at a rate of 1.99%, as opposed to 1.51% for other patients.

72. In March 2007, GSK obtained an advance copy of the Nissen/Wolski Study from a peer review editor of the article, even though the article was confidential. *See* Staff Report On GlaxoSmithKline And The Diabetes Drug Avandia, Committee Print, 111th Congress 2d Sess., S. Prt. 111-41 at 3 (January 2010) ("Staff Report"). "According to documents produced by GSK, the leaked manuscript was widely disseminated within the Company, and allowed GSK to launch a public relations plan to protect Avandia, a multi-billion dollar product." *Id.* Company documents indicated that "over 40 executives at GSK received and/or learned of the results in the leaked study." *Id.*

73. GSK's own statistician concluded that "there is no statistical reason for disregarding the findings as presented" and noted that previous studies were consistent with the article's findings. *Id.* at 6. **(**citing Internal GSK document, "Report on the article by SE Nissen & K Wolski 'Effect of rosiglitazone on the risk of myocardial infarction and cardiovascular death.'" Research Statistic Unit, GSK, DRAFT May 4, 2007)). Furthermore, the Nissen study was consistent with the 2005 and 2006 trials commissioned by GSK.

74. Nonetheless, on the same day that the study was published on May 21, 2007, GSK publicly stated that it "strongly disagrees with the conclusions reached in the *NEJM* article, which are based on incomplete evidence and a methodology that the author admits has significant limitations." GlaxoSmithKline Press Release: "GlaxoSmithKline responds to NEJM article on Avandia," published online May 21, 2007. Instead, GSK highlighted the results of company-sponsored trials like RECORD as "the most scientifically rigorous way to examine the safety and benefits of a medicine." *Id.*

75. In a letter to *The Lancet*, GSK maintained that the RECORD trial is ''compelling evidence'' for the safety of Avandia. Ronald Krall M.D., Chief Medical Officer,

GlaxoSmithKline, ‘‘Cardiovascular Safety of Rosiglitazone,’’ *The Lancet*, letter published online May 30, 2007.

76. In fact, GSK's presentation of its RECORD trial was dimly viewed by *NEJM* reviewers and editors. *See* Staff Report at 4, 8-10. Concerning the comments of one reviewer, the editors wrote that for myocardial infarction, the "estimates in the RECORD trial and the Nissen meta-analysis" overlap in their confidence intervals, meaning that they found a similar trend for heart attacks. *Id.* at 9. "The editors [felt] strongly that [GSK's] data d[id] not support the statement that the RECORD results for MI contradict the Nissen meta-analysis" and thus, that "this statement must be removed or modified." *Id*. at 9-10. An editorial by the *NEJM* questioned the RECORD Study, as well as other Avandia studies such as DREAM and ADOPT. *Id*. at 10.

Post- Nissen/Wolski Study

77. Following publication of the Nissen/Wolski study, the FDA issued a safety alert for Avandia on May 21, 2007, addressing safety issues based on analysis of controlled clinical trials demonstrating a potentially significant increase in the risk of heart attack and heart-related diseases in patients treated with Avandia.

78. On May 23, 2007, the FDA issued letters to GSK requesting that Avandia's label include a black box warning to more prominently address the risks of heart failure associated with its use.

79. Despite all these warnings and FDA admonitions, GSK engaged in large-scale publication and advertising designed to down-play the risks and assure consumers of Avandia's safety, including full-page newspaper advertisements touting Avandia in June 2007. This advertising and marketing included promotional literature for doctors and other health care providers, as well as direct-to-consumer materials.

FDA Reaction to Nissen/Wolski

80. On July 30, 2007, the Endrocrinologic and Metabolic Drugs Advisory Committee, and Drug Safety and Risk Management Advisory Committee of the FDA convened to evaluate the safety of Avandia.

81. At the hearing, the FDA presented the results of its own meta-analysis. Similar to the previous findings, the FDA likewise found an increased risk of heart attack, cardiovascular death, stroke and other serious ischemic related adverse events and ultimately recommended that a boxed warning be placed on the Avandia label.

82. Specifically, Dr. David Graham, FDA Office of Surveillance and Epidemiology, presented results of the FDA's meta-analysis of Avandia at the July 30 hearing, including: (1) the FDA meta-analysis showed a 20%-60% increased cardiovascular risk with six to twelve months of Avandia use compared to non-use; (2) Avandia increased risk of ischemic heart disease by 40% compared with comparator drugs and by 70% compared with placebo; (3) compared to pioglitazone (Actos), Avandia increases the risk of a cardiovascular event over three and one-half times; (4) the data indicates that since it was introduced to the market, Avandia use caused between 66,000 and 205,000 cardiovascular events that otherwise would not have occurred.

83. Dr. Graham called for withdrawing Avandia from the market. Dr. Graham estimated that there were between 66,000 and 200,000 excess cases of cardiovascular events, some fatal, attributable to Avandia since 1999. *See* FDA Advisory Committee Hearing Transcript dated July 30, 2007 at 229-231, 236. Referring to cardiovascular adverse events, including heart attack, Dr. Graham stated that "[t]here is no evidence, none whatsoever, to support the benefits of rosiglitazone with these outcomes." *Id*. at 231.

84. Additional testimony was presented by Dr. Sidney Wolfe, Elizabeth Barbehenn, Ph.D., and Ben Wolpaw (members of Public Citizen's Health Research Group) that many of the early signals of Avandia's significant cardiac adverse effects included a 1999 FDA pharmacology review of animal toxicity in rosiglitazone use and anticipated potential human toxicities, leading the FDA pharmacologist to recommend against approving rosiglitazone for long-term human use. Additional testimony was presented that the receptor on which Avandia acts causes cardiac cells to produce and store fat, resulting in disruption of myocardial contraction and heart disease and failure.

85. The FDA provided testimony that Avandia offers no unique benefits for controlling diabetes compared to other drugs, but that all indications point to increased risks of heart attack and sudden death. *See, e.g., id.* at 232 ("So, we see that there are no major health benefits demonstrated for rosiglitazone, neither macrovascular benefits nor microvascular benefits. We also see no evidence that rosiglitazone confers any advantage over other oral anti-diabetes treatments for a variety of intermediate outcomes. Finally, rosiglitazone confers no unique advantage over pioglitazone and appears to be inferior to pioglitazone with respect to some intermediate outcomes"); *see also id.* at 234-235 ("For a health benefit to justify a serious risk, we believe that it must be clinically important and meaningful. It must be of comparable or greater health value to patients, and occur with a greater frequency than the risk, and there must be definitive evidence or very strong evidence to support that benefit . . . There is absolutely no evidence of a major clinical health benefit with rosiglitazone").

86. At the July 30 Hearing, the FDA Joint Advisory Committee made the non-binding recommendation that Avandia should remain on the market, but also voted 20-to-3 that the data

showed an increase in cardiovascular risks associated with Avandia. The committee urged that GSK be required to add a black box warning to Avandia's label.

87. On August 14, 2007, the FDA issued a press release indicating that GSK had agreed to add a black box label concerning the risk of heart failure. According to the press release: "The upgraded warning emphasizes that [Avandia] may cause or worsen heart failure in certain patients."[2] The black box warning for Avandia stated that "Thiazolidinediones, including rosiglitazone, cause or exacerbate congestive heart failure in some patients."[3]

88. In November 2007, however, the FDA in connection with GSK's revised labeling for Avandia concerning the risks of myocardial ischemic events (including heart attacks) stated in part that: "A meta-analysis . . . showed Avandia to be associated with an increased risk of myocardial ischemic events such as angina or myocardial infarction. Three other studies . . . have not confirmed or excluded this risk. In their entirety, the available data on the risk of myocardial ischemia are inconclusive." [4]

89. Subsequently, in September 2010, the FDA announced that it would require GSK to develop a restricted access program for Avandia under a risk evaluation and mitigation strategy ("REMS") under which Avandia would be available to new patients "only if they are unable to achieve glucose control on other medications and are unable to take Actos (pioglitazone), the only other drug in this class." FDA News Release dated September 23, 2010.[5]

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[2] http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ 2007/ucm108966.htm.

[3]http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM143413.pdf.

[4]http://www.fda.gov/newsevents/newsroom/pressannouncements/2007/ucm109026.htm

[5] During this same time period, other regulators also were taking action. In September, 2010, the European Medicines Agency announced it was suspending marketing authorization for rosiglitazone.

90. The FDA also directed that GSK convene an independent group of scientists to review key aspects of the company's clinical trial known as RECORD, which studied the cardiovascular safety of Avandia compared to standard diabetes drugs. The FDA stated in its September 23, 2010 News Release that: "During the course of the FDA's review of the RECORD study, important questions arose about potential bias in the identification of cardiovascular events. The FDA is requiring this independent review to provide additional clarity about the findings." *Id.*

91. In May 2011, the FDA announced new restrictions to the prescribing and use of rosiglitazone-containing medicines sold under the names Avandia, Avandamet, and Avandaryl. The FDA modified the REMS for Avandamet and Avandaryl which previously "consisted of only a Medication Guide" to include a restricted access and distribution program, applied to all three rosiglitazone products. FDA Safety Announcement, "FDA Drug Safety Communication: Updated Risk Evaluation and Mitigation Strategy (REMS) to Restrict Access to Rosiglitazone-containing Medicines including Avandia, Avandamet, and Avandaryl," May 18, 2011.

The FDA Halted the TIDE Study Due to Avandia Safety Concerns

92. In 2007, "the FDA asked GSK to perform a cardiovascular safety trial, called TIDE (Thiazolidinedione Intervention With Vitamin D Evaluation), to compare Avandia to other diabetes treatments such as ACTOS (piolglitazone)" and that "[i]n response to several document requests made to the FDA, we received and reviewed an analysis conducted by two FDA safety officials" in October 2008 which stated, among other things that: "[T]here is no evidence that rosiglitazone confers any unique health benefits over pioglitazone while there is strong evidence that rosiglitazone confers an increased risk of [heart attacks] and heart failure compared to pioglitazone." *Id.* The safety officer wrote that because of cardiovascular concerns with

Avandia, "the safety of the study itself cannot be assured, and is not acceptable." *Id.* Letter to Margeret A. Hamburg, Commissioner of the FDA from Max Baucus and Chuck Grassle dated February 18, 2010.

93. The FDA considered whether to stop the TIDE study amid concern by FDA scientists that it was "unethical to compare a drug with known cardiac risks with a seemingly safer alternative. They also say Avandia should be pulled from the market." FDA Weighs Halting Avandia Safety Study, *Wall Street Journal* (April 19, 2010).

94. Approximately July 2010, the FDA advised GSK that the TIDE study had been placed on partial clinical hold under which no new patients would be accepted into the study.

95. Ultimately, the FDA halted the TIDE study and rescinded all of the regulatory deadlines for completion of the trial. *Id.*

Numerous Other Studies Corroborated Avandia's Risks

96. In September 2007, the Journal of the American Medical Association published a study (consisting of yet another meta-analysis) finding that Avandia doubled the risks of heart failure and raised the risk of heart attack by 42%. *See* S. Singh, et al., "Long Term Risk of Cardiovascular Events with Rosiglitazone," Journal of the American Medical Association 298:189-1195 (September 12, 2007).

97. Another Canadian study examined "real-world data" and concluded that "TZD treatment was associated with a significant increase in the risks of CHF, AMI, and all-cause mortality among older persons with diabetes compared with other oral diabetes treatment" and that "[t]he association between TZD treatment and cardiovascular events appeared to be limited to rosiglitazone. Our findings are consistent with recent studies that showed an increase in AMI risk and possibly death with rosiglitazone." Lipscome, et al., "Thiazolidinediones and Cardiovascular Outcomes in Older Patients with Diabetes," Journal of the American Medical

Association, 298(2): 2634-2643 (December 12, 2007). "Our large, well-designed population-based study provides more convincing evidence that rosiglitazone is associated with an increased risk of cardiac events and deaths among elderly patients with diabetes. Moreover, . . . the magnitude of association between TZDs and adverse outcomes was consistent with risks reported elsewhere. For example, both rosiglitazone meta-analyses reported an approximate 40% increased risk of AMI compared with placebo, which is similar to the risk increase in our study." *Id.*

98. In October 2008, Public Citizen petitioned the FDA to ban Avandia based on evidence of increase risk of heart attack, heart failure and other adverse events. The petition also stated that the issue is furthered by the lack of evidence of any clinical benefit compared to other approved drugs for diabetes such as metformin, insulin and sulfonylureas.[6]

99. A May 6, 2009 study showed that Avandia increases apoBlevels, increases LDL particle numbers, and increased apoB levels' association with cardiovascular risks in Type II diabetes. *See* Martin et al., "Apolipoprotein B but not LDL Cholesterol is Associated with Coronary Artery Calcification in Type 2 Diabetic Whites," The American Diabetes Association 58: 1887-1892 (2009). GSK did not warn either patients or doctors of the increased apoB levels contributing to cardiovascular events.

100. Another February 2010 study published in the Journal for the American Diabetes Association, Diabetes Care, found that Avandia increases a diabetic's heart attack risk by 30% compared with the older drug sulfonylurea, and that when compared with metformin, Avandia increases a diabetic's heart attack risk by 120%.

[6] Petition to Ban Diabetes Drug Rosiglitazone (Avandia), October 30, 2008 (http://www.citizen.org/Page.aspx?pid=610).

101. As reported in *Bloomberg*, July 9, 2010, Dr. Rosemary Johann-Liang, a former manager in the FDA's drug-safety unit[7], revealed that a 2001 study found Avandia posed a greater heart-attack risk than rival medicines and that GSK did not provide the FDA with an email from researchers who concluded that Avandia "strengthens the signals" of heart ailments.

102. Other studies also have concluded that Avandia provides no better benefit to preventing heart attacks or stroke than other treatments. *See* Annals of Internal Medicine, September 2007 (concluding that when compared with newer agents such as Avandia, older agency "have similar or superior effects on glycemic control, lipids, and other intermediate endpoints"); Keith J. Winstein, "Diabetes Study Questions Expensive Treatments: NIH Finds Patients With Heart Disease Fare Equally Well Without Stents and Drugs Such as Avandia, Actos," *Wall Street Journal* June 8, 2009 (reporting on diabetes study sponsored by National Institutes of Health and drug companies concluding that aggressive use of drugs like Avandia perform no better in preventing deaths, heart attacks or strokes than other treatments such as insulin).

103. Another study also revealed adverse events in 98% of persons taking Avandia. This study reported an approximate 24% increase in LDL cholesterol and a 10% decrease in HDL (high-density lipoprotein) levels after 12 weeks. *See* A 12-Week Randomized, Double-Blind, Local Multicenter, Placebo-Controlled Study To Evaluate The Efficacy, Sfety And Tolerability Of Rosiglitazone (BRL 49653C) When Administered Once Daily To Patients With Type-2 Diabetes Mellitus (T2DM) Who Are Inadequately Controlled On At Least Half Maximal Dose Of Usual Sulphonylurea."

[7] In a statement published in late July, 2007, Senator Chuck Grassley revealed that Rosemary Johann-Liang, had recommended a black box warning for Avandia in February 2006, but that the FDA removed her from work on Avandia after she had voiced concerns and did not act on her advice. Rita Rubin, *FDA Scientist Says She Was Reprimanded For Warning*, USA Today, June 12, 2007; *see also* Ed Silverman, *Avandiagate: FDA Reviewer Walks The Plank*, pharmalive.com, June 11, 2007.

Congressional Reaction to Warnings Concerning Avandia

November 2007 Report

104. In November 2007, the U.S. Senate Committee on Finance issued a Staff Report calling GSK's response to Dr. Buse's earlier concerns "extremely serious," and stated that it revealed an "orchestrated plan to stifle the opinion" of a diabetes specialist. *See* Committee Staff Report to the Chairman and Ranking Member, Committee on Finance, United States Senate, "The Intimidation of Dr. John Buse and the Diabetes Drug Avandia," dated November 2007.

105. The Committee Staff Report also expressed concerns that GSK had not altered its corporate culture in the years since the attacks on Dr. Buse (1999-2000) because "GSK's behavior since the Committee first brought these allegations to light has been less than stellar. Instead of acknowledging the misdeed to investors, apologizing to patients and pledging to change its corporate behavior, GSK launched a public relations campaign of denial." *Id.*

January 2010 Report

106. In January 2010, the United States Senate Committee on Finance issued a Staff Report on Avandia after reviewing over 250,000 documents and conducting several interviews. *See* Staff Report at 1.

107. Regarding GSK's response to the Nissen/Wolski study, the Committee found that GSK's public reaction was disingenuous. The Staff Report stated: "The company's own experts analyzed the [Nissen/Wolski] study, found it to be statistically reliable, and then attacked the soundness of that study in press releases and public comments." *Id.*

108. The Staff Report outlined GSK's conduct and concluded: "The totality of evidence suggests that GSK was aware of the possible cardiac risks associated with Avandia years before such evidence became public. Several years prior to Nissen's study, it can be argued that GSK was on notice that Avandia may have problems. Based on this knowledge, GSK had a

duty to sufficiently warn patients and the FDA of its concerns in a timely manner. Instead, GSK executives intimidated independent physicians, focused on strategies to minimize findings that Avandia may increase cardiovascular risk, and sought ways to downplay findings that the rival drug . . . might reduce cardiovascular risk." Staff Report at 15.

109. The Staff Report revealed that GSK was aware, since at least 2004, that the RECORD trial (cited by GSK as a basis for discrediting the Nissen analysis) was statistically inadequate to address issues regarding cardiovascular safety and that "inconclusive" results could be favorable to GKS and its marketing strategy for Avandia. *Id.* at 4

110. According to a February 22, 2010 *New York Times* article, the congressional investigation found internal emails regarding GSK's statistician's conclusion that there was "no statistical reason for disregarding the findings" of Dr. Nissen's study. In another, Mr. Moncef Slaoui, head of research for GSK, wrote that federal drug regulators, Dr. Nissen, and the company's own researchers all seem to agree that studies of Avandia showed that it substantially increases the risk of death and heart attacks (ischemic events): "F.D.A., Nissen and G.S.K. all come to comparable conclusions regarding increased risk for ischemic events, ranging from 30 percent to 43 percent!"

Recent Enforcement Action by the Department of Justice

111. In July 2012, the Justice Department announced that GSK agreed to plead guilty and to pay $3 billion to resolve criminal and civil liability arising from, among other things, unlawful promotion of certain prescription drugs, and failure to report certain safety data. *See* Department of Justice Office of Public Affairs News Release dated July 2, 2012.

112. GSK pleaded guilty to failing to report data to the FDA (and to pay a criminal fine in the amount of $242,612,800) for unlawful conduct concerning Avandia in response to

allegations that "between 2001 and 2007, GSK failed to include certain safety data about Avandia, a diabetes drug, in reports to the FDA that are meant to allow the FDA to determine if a drug continues to be safe for its approved indications and to spot drug safety trends. The missing information included data regarding certain post-marketing studies, as well as data regarding two studies undertaken in response to European regulators' concerns about the cardiovascular safety of Avandia." *Id*.

113. In the civil settlement agreement, the United States alleged "that GSK promoted Avandia to physicians and other health care providers with false and misleading representations about Avandia's safety profile, . . . [specifically] that GSK stated that Avandia had a positive cholesterol profile despite having no well-controlled studies to support that message. The United States also alleges that the company sponsored programs suggesting cardiovascular benefits from Avandia therapy despite warnings on the FDA-approved label regarding cardiovascular risks." GSK agreed to pay $657 million relating to false claims arising from misrepresentations about Avandia. *Id.*

GSK Misrepresented and Omitted Material Facts About Avandia

114. Despite all the studies and warnings about Avandia's risks, GSK has from the time Avandia was approved, engaged in widespread marketing and advertising to promote Avandia to physicians, consumers, and others as safe and effective. GSK also has actively concealed and/or suppressed material information about Avandia's risks through, among other things, its sales representatives and badly designed studies. GSK's concealment extended even to the FDA.

115. In connection with the sale or advertising of Avandia, GSK used or employed deception, false pretense, false promise, misrepresentation, unfair practice and/or concealed,

suppressed, or omitted material facts. Despite its own internal studies that suggested otherwise, Avandia misrepresented the risks associated with Avandia, and it omitted material facts that it knew or reasonably should have known concerning those risks.

116. For example, in addition to the other instances described herein, GSK's internal studies reflected an increased cardiovascular risk associated with Avandia, and GSK had information that corroborated the Nissen/Wolski article. Yet, on June 1, 2007, GSK published a "Dear Avandia Patient" letter, which responded to the "recent press coverage about the safety of Avandia." Therein, GSK stated that it "stands firmly behind Avandia," that "Avandia is the most widely studied medicine for type II diabetes" and that the evaluation of clinical trials by "well-informed experts and researcher has been encouraging."

117. Additionally, in December 2007, GSK issued a press release stating: "Across multiple sources of data, there is no consistent or systematic evidence that rosiglitazone increases the risk of myocardial ischemic events or deaths in comparison to other anti-diabetic agents." Press Release, "GlaxoSmithKline responds to JAMA article on the ICES thiazolidinediones and cardiovascular outcomes in older patients with diabetes, December 11, 2007.

118. Thus, despite notice of the dangerous propensities associated with Avandia, GSK engaged in misrepresentations, and failed to adequately advise consumers and medical providers of the risks of Avandia, including but not limited to the increased risk of heart attacks and deaths. Furthermore, the company omitted material facts concerning Avandia's risk factors, even though it knew or reasonably should have known those facts. GSK also promoted Avandia's efficacy when in fact, Avandia is no more effective than other drugs.

119. Staci Laurino purchased and used Avandia as early as 2007, which had been prescribed for her by a licensed physician, and she used it as prescribed.

120. GSK misrepresented, concealed, suppressed and/or omitted material facts concerning Avandia and the fact that the drug increased the likelihood of cardiovascular disease.

121. Contrary to GSK's advertising and promotion, Avandia is not more efficacious than other treatments for Type II diabetes and significantly increases the risk of heart-related diseases including heart attack and stroke

122. The actual value of Avandia was/is significantly less than the value of Avandia as represented by GSK, and thus, Plaintiff and other consumers suffered ascertainable loss when they purchased Avandia.

ALLEGATIONS RELATED TO PUNITIVE DAMAGES

123. Plaintiff incorporates by reference the allegations in all paragraphs of this Amended Complaint as though fully set forth in this paragraph.

124. GSK's unlawful practices including unfair practices, deception, false promises, false pretense, misrepresentation, and/or the concealment, suppression, or omission of material facts in connection with the sale, distribution or advertisement of Avandia were outrageous because of GSK's evil motive and/or conscious disregard and/or reckless indifference to the rights and/or safety of Plaintiff, Class members, and others.

125. As a result of GSK's conduct alleged herein, the jury should be permitted to return a verdict of punitive damages under Count I of this Amended Complaint that will serve to punish Defendant and deter Defendant and others from like conduct. The MMPA expressly provides for punitive damages. *See* Mo. Rev. Stat. § 407.025.

CLASS ACTION ALLEGATIONS

126. Plaintiff incorporates by reference the allegations in all paragraphs of this Amended Complaint as though fully set forth in this paragraph.

127. Plaintiff brings this class action pursuant to Federal Rule of Civil Procedure 23 on behalf of herself and the following class of similarly situated persons:

> All Missouri residents who purchased Avandia for personal or family use, and other persons who purchased Avandia in Missouri for personal or family use (and their estates, administrators, legal representatives, heirs or beneficiaries).

128. Excluded from the class are the officers, directors, agents or employees of Defendant or any parent, subsidiary, or affiliate of Defendant; the judicial officers assigned to this litigation, as well as members of their staffs and immediate families. Also excluded from the class is any individual who has asserted a claim for personal injury as a result of taking Avandia as to such injury.

129. The proposed class meets all requirements for class certification. The proposed class satisfies the numerosity standards. The class is believed to number in the thousands of persons in the state of Missouri. As a result, joinder of all class members in a single action is impracticable.

130. There are questions of fact and law common to the class which predominate over any questions affecting only individual members. The questions of law and fact common to the class include, without limitation, the following:

(a) whether, in connection with advertising or selling Avandia, Defendant failed to disclose the dangers and risks to the health of persons ingesting the drug;

(b) whether in connection with marketing or selling Avandia, Defendant falsely and fraudulently misrepresented in its advertisements, promotional materials or elsewhere, the safety, potential side effects, and/or efficacy of Avandia;

(c) whether in connection with marketing or selling Avandia, Defendant engaged any method, act, use, practice, advertisement or solicitation having the tendency or capacity to mislead, deceive or cheat, or that tends to create a false impression in regard to the safety, potential side effects and/or efficacy of Avandia;

(d) whether, in connection with marketing or selling Avandia, Defendant made any assertions not in accord with the facts in regard to the safety, potential side effects and/or efficacy of Avandia;

(e) whether, in connection with marketing or selling Avandia, Defendant omitted any material fact necessary in order to make statements made, in light of the circumstances under which they were made, not misleading;

(f) whether in connection with marketing or selling Avandia, Defendant failed to disclose material facts either known to it or that, upon reasonable inquiry would be known to it;

(g) whether Defendant failed to warn adequately of the adverse effects of Avandia;

(h) whether Defendant knew or could have known that the use of Avandia leads to serious adverse health effects;

(i) whether Defendant adequately tested Avandia prior to, and during distribution and sales in the market place;

(j) whether Defendant continued to manufacture, market, distribute, and sell Avandia notwithstanding its actual or constructive knowledge of the drug's dangerous nature;

(k) whether in connection with marketing or selling Avandia, Defendant engaged any method, act, use or practice that operated to hide or keep material facts from consumers;

(l) whether in connection with marketing or selling Avandia, Defendant engaged in any method, act, use or practice likely to curtail or reduce the ability of consumers to take notice of material facts which were stated;

(m) whether Defendant's conduct violated Missouri's Merchandising Practices Act; and

(n) whether the actual value of Avandia was less than the value of Avandia as represented by Defendant.

131. The questions set forth above predominate over any questions affecting only individual persons, and a class action is superior with respect to considerations of consistency,

economy, efficiency, fairness and equity, to other available methods for the fair and efficient adjudication of this controversy.

132. A class action is the appropriate method for the fair and efficient adjudication of this controversy. The presentation of separate actions by individual class members could create a risk of inconsistent and varying adjudications, establish incompatible standards of conduct for Defendant, and/or substantially impair or impede the ability of class members to protect their interests.

133. Plaintiff is an adequate representative of the class because she is a member of the class and her interests do not conflict with the interests of the members of the class that she seeks to represent. The interests of the members of the class will be fairly and adequately protected by Plaintiff and her undersigned counsel, who have extensive experience prosecuting complex class action litigation.

134. On behalf of herself and the class, Plaintiff seeks damages equal to the difference between the actual value of Avandia and the value of Avandia had it been as represented by Defendant.

135. Maintenance of this action as a class action is a fair and efficient method for the adjudication of this controversy. It would be impracticable and undesirable for each member of the class who suffered harm to bring a separate action. In addition, the maintenance of separate actions would place a substantial and unnecessary burden on the courts and could result in inconsistent adjudications, while a single class action can determine, with judicial economy, the rights of all class members.

136. Notice can be provided to class members by using techniques and forms of notice customarily used in drug-related cases and complex class actions, including by published and broadcast notice.

CLAIM FOR RELIEF
COUNT I
VIOLATION OF THE MISSOURI MERCHANDISING PRACTICES ACT

137. Plaintiff incorporates by reference the allegations in all paragraphs of this Amended Complaint as though fully set forth in this paragraph.

138. As a result of Defendant's actions, Avandia sales were an enormous source of profits for Defendant and accordingly, Defendant had a significant financial incentive to suppress, misrepresent omit and/or conceal any potential dangers or risks associated with Avandia.

139. Defendant acted for the purpose of maximizing profits at the expense of, and notwithstanding the very real risk to others.

140. In connection with the advertising, marketing, sale, and distribution of Avandia, Defendant engaged in the acts and practices including deception, false promises, misrepresentation, and/or the concealment, suppression, or omission of material facts, each of which constitutes an unlawful and/or unfair practices in violation of the Missouri Merchandising Practices Act, Mo. Rev. Stat. §§ 407.010 *et seq.*

141. In addition to the affirmative misrepresentations outlined herein in violation of the Missouri Merchandising Practices Act, Defendant also omitted material facts in violation of the statute in that Defendant failed to disclose material facts known to it, or upon reasonable inquiry would be known to it.

142. In addition, Defendant engaged in unfair practices that either (1) offend public policy; (2) are unethical, oppressive or unscrupulous; (3) or present a risk of or cause substantial injury to consumers in violation of the Missouri Merchandising Practices Act. *See* 15 CSR § 60-8.020

143. Defendant also engaged in methods, use or practices which violate state or federal law intended to protect the public and present a risk of, or cause substantial injury to consumers in violation of the Missouri Merchandising Practices Act. *See* 15 CSR § 60-8.090.

144. As a result of purchasing Avandia, Plaintiff and the class suffered ascertainable loss.

145. Punitive damages are warranted in this case based on Defendant's evil motive and/or conscious disregard and/or reckless indifference to the rights and/or safety of Plaintiff, class members, and others.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff requests that this Court enter judgment against Defendant and in favor of Plaintiff and award the following relief:

(a) Certification of the proposed class;

(b) Damages suffered by Plaintiff and the class;

(c) Attorneys' fees and those costs available under the law; and

(d) Punitive damages in an amount sufficient to punish Defendant and deter Defendant and others from like conduct in the future.

JURY DEMAND

Plaintiff hereby demands a trial by jury on all claims so triable.

Date: November 14, 2013

Respectfully submitted,

STUEVE SIEGEL HANSON LLP

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CERTIFICATE OF SERVICE

I hereby certify that on November 14, 2013, I filed the foregoing document via the Court's ECF system, which will cause a true and correct copy of the same to be served electronically on all ECF-registered counsel of record.

/s/ Patrick J. Stueve
Counsel for Plaintiff